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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,736	07/19/2007	Sophie Lotersztajn	EPLDUB090536USAF/903002US	9624

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,736	LOTERSZTAJN ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2010*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,12-15,17 and 19-27* is/are pending in the application.

4a) Of the above claim(s) *12-14,20,22 and 24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,15,17,19,21,23 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's amendment/remarks filed 01/19/2010. By the amendment, claim 17 has been amended and claim 18 has been cancelled.

2. In response to applicant's argument that "N-piperidino-5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-4-ethylpyrazole-3-carboxamide or one of its pharmaceutically acceptable salt" recited in claim 20 which depends from amended claim 17 is improperly withdrawn and should be examined along with the elected species, the examiner recognizes the applicant's election of N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide as the elected species (Response filed 07/14/2009).

The species recited in claim 20 is not readable on the elected species even though the elected species differs from the claim 20 species only by the substitution of a similar element at the same position on the ring. Furthermore, there is no statement on the current record that the species in recited in claim 20 is obvious variants to the elected species. Thus, it is proper to withdraw such claim from further examination as being drawn to non-elected invention.

3. Applicant's amendment changing the scope of the invention by requiring "consisting essentially of" necessitates a new ground(s) of rejection in this Office Action. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

4. Claims 2, 15, 17, 19, 21, 23 and 27 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 2, 15, 17, 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Batkai et al. (Nature Medicine, Volume 7, No. 7, 2001, pp.827-832).

Batkai teaches an administration of CB1 receptor antagonist such as SR141716A (commonly known N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide or rimonabant) to an animal having the advanced cirrhosis associated with the vasodilated state, wherein said SR141716A is administered in 3mg/kg (abstract; page 827, column 2, last paragraph to page 829, column 1, 1st paragraph; Discussion). Batkai teaches that the activation of vascular CB1 receptor is involved in pathophysiology of liver cirrhosis and the antagonist of CB1 receptor is useful in providing a therapeutic utility in managing patients with advanced liver cirrhosis awaiting liver transplantation.

With respect the instant "from 0.01 mg to 500mg" recited in claim 15, the examiner determines that the referenced 3mg/kg (e.g., average weight of approx. 200g of rat is translated to approx. 0.6mg) falls within the "metes and bounds" of the instant claimed dosage range. Thus, the reference anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Batkai et al. (Nature Medicine, Volume 7, No. 7, 2001, pp.827-832) in view of Shakkebaek et al. (US 5492891).

The teaching of Batkai has been discussed in above 35 USC 102(b) rejection.

The teaching of Batkai differs from the claimed invention because rimonabant is not specifically named for the treatment of alcoholic liver cirrhosis.

Shakkebaek is being provided as a supplemental reference to demonstrate nexus between alcoholic abuse and cirrhosis of liver development. (column 1, lines 10-32).

However, one having ordinary skill in the art would have expected as taught by Batkai that compounds having CB1 receptor antagonist activity would be useful in the treatment of cirrhosis of the liver, which is usually develops as a long-term consequence of chronic alcohol abuse or viral hepatitis, particularly advanced cirrhosis of the liver associated with vasodilated sate (which contributes to portal hypertension and the development of ascites). One having ordinary skill in the art would have expected per view of Batkai and Shakkebaek combination that compounds having CB1 receptor antagonist activity would be useful in the treatment of cirrhosis of the liver induced by alcoholism or alcohol addiction.

With respect to the specific dosage amounts of CB1 receptor antagonist recited in claim 27, those of ordinary skill in the art would have been readily optimized effective dosage amounts as determined by good medical practice and the clinical condition of the individual patient. One having ordinary skilled in the art would have been motivated to make such modification to extend the usage of said composition in oral dosage forms, particularly solid dosage form, to accommodate patient's preference and needs where the compliance could be improved with effective and well tolerated drug.

Regardless of the manner of administration, the specific dose would have been calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage for treatment involving each of the above

mentioned formulations would have been routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation. Furthermore, the final dosage regimen would have been determined by the attending physician, considering the drug's specific activity, the responsiveness of the subject, the age, condition, body weight and diet, the severity of any infection, time of administration and other clinical factors. Given the teachings in the state of art, those of ordinary skill would be able to determine appropriate dosage amounts of the CB1 receptor antagonist having optimum therapeutic index, and would be motivated to determine optimum amounts to maximize the efficacy of drugs.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614